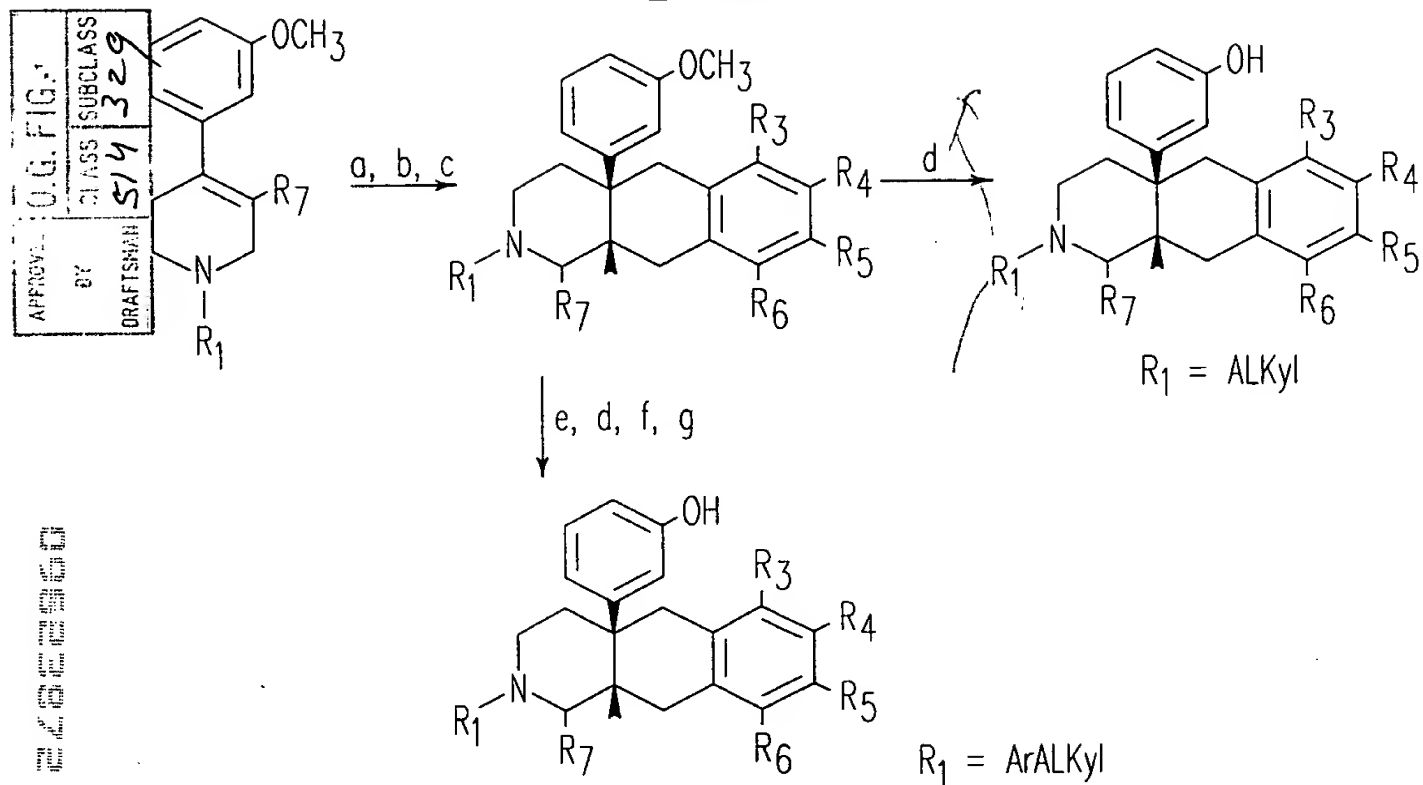
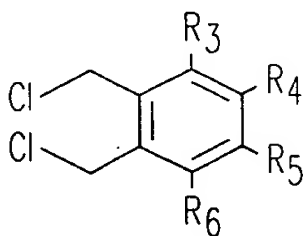


FIG. 1



Reagents: (a) *s*-BuLi, THF; AND



(b) NaI, CH<sub>3</sub>CN;

(c) NaBH<sub>4</sub>, EtOH;

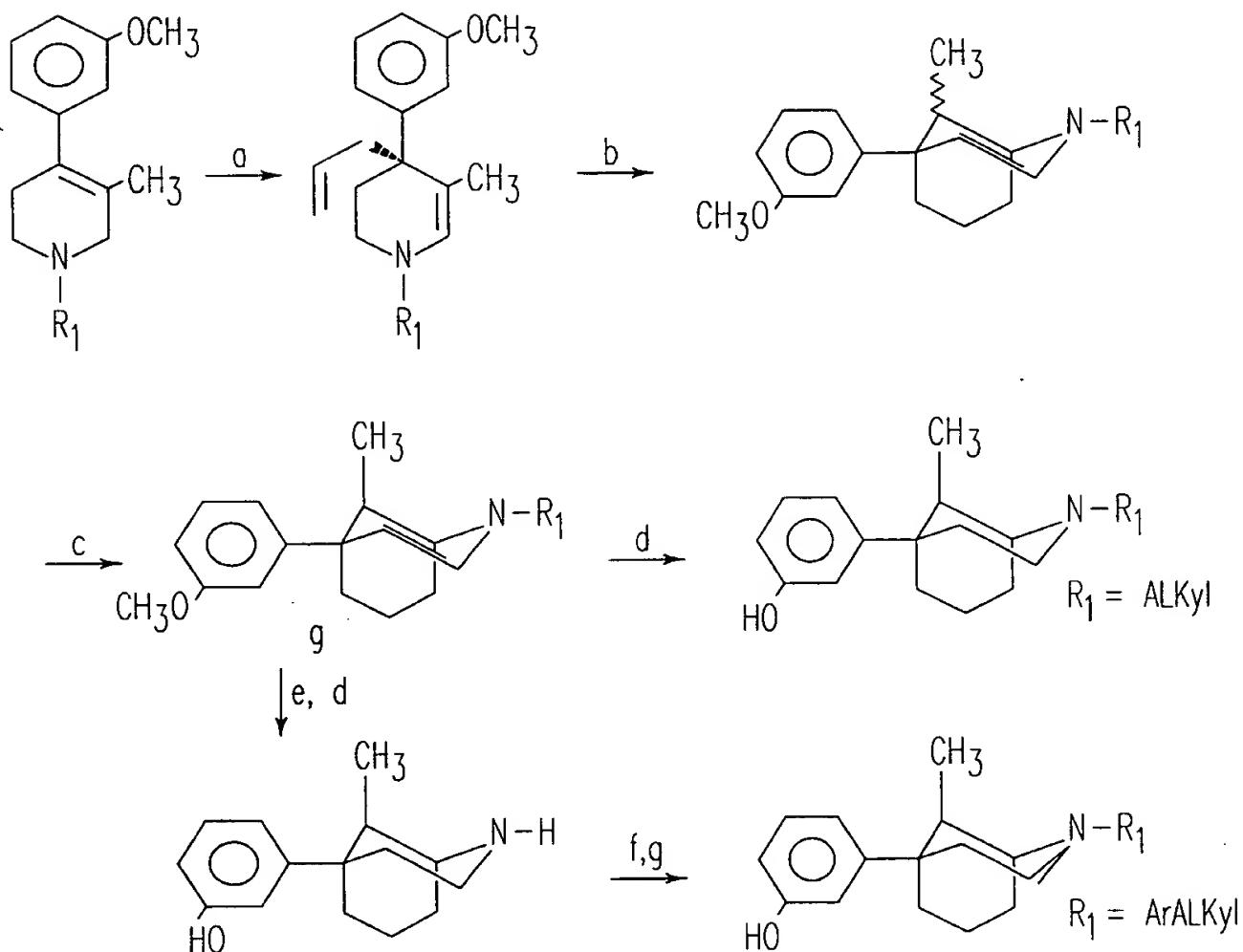
(d) HBr, HOAc;

(e) PhOCOCi, toluene;

(f) aryl-alkyl-COOH, BOP, triethylamine, THF,

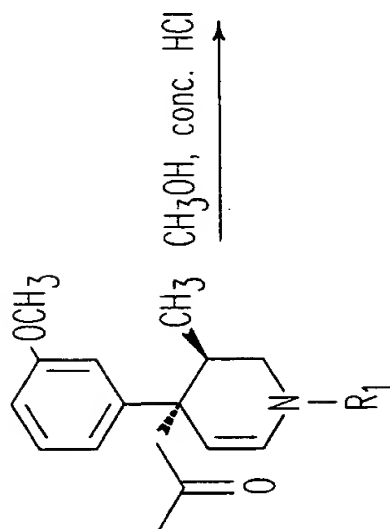
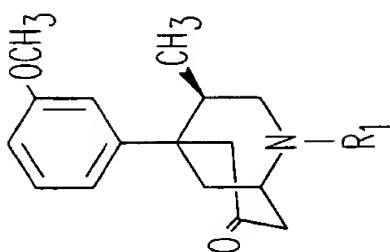
(g) borane/THF

FIG. 2A

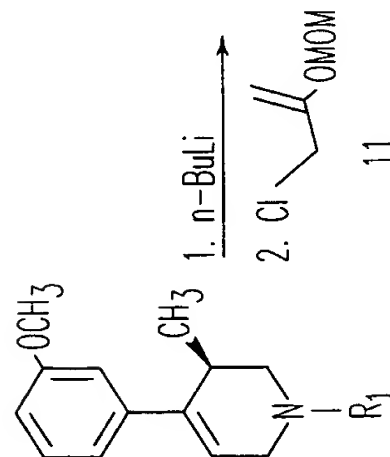


APPROVE	C.G. FIG.
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FIG. 2B



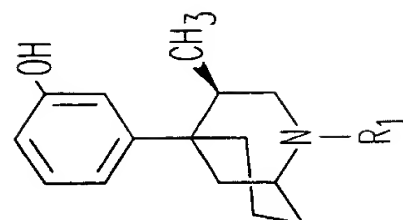
CH<sub>3</sub>OH, conc. HCl



1. n-BuLi  
2. Cl-CH<sub>2</sub>-CH=CH-OMOM

11

3. 2N HCl



1. Zn, HCl  
2. HBr, HOAc

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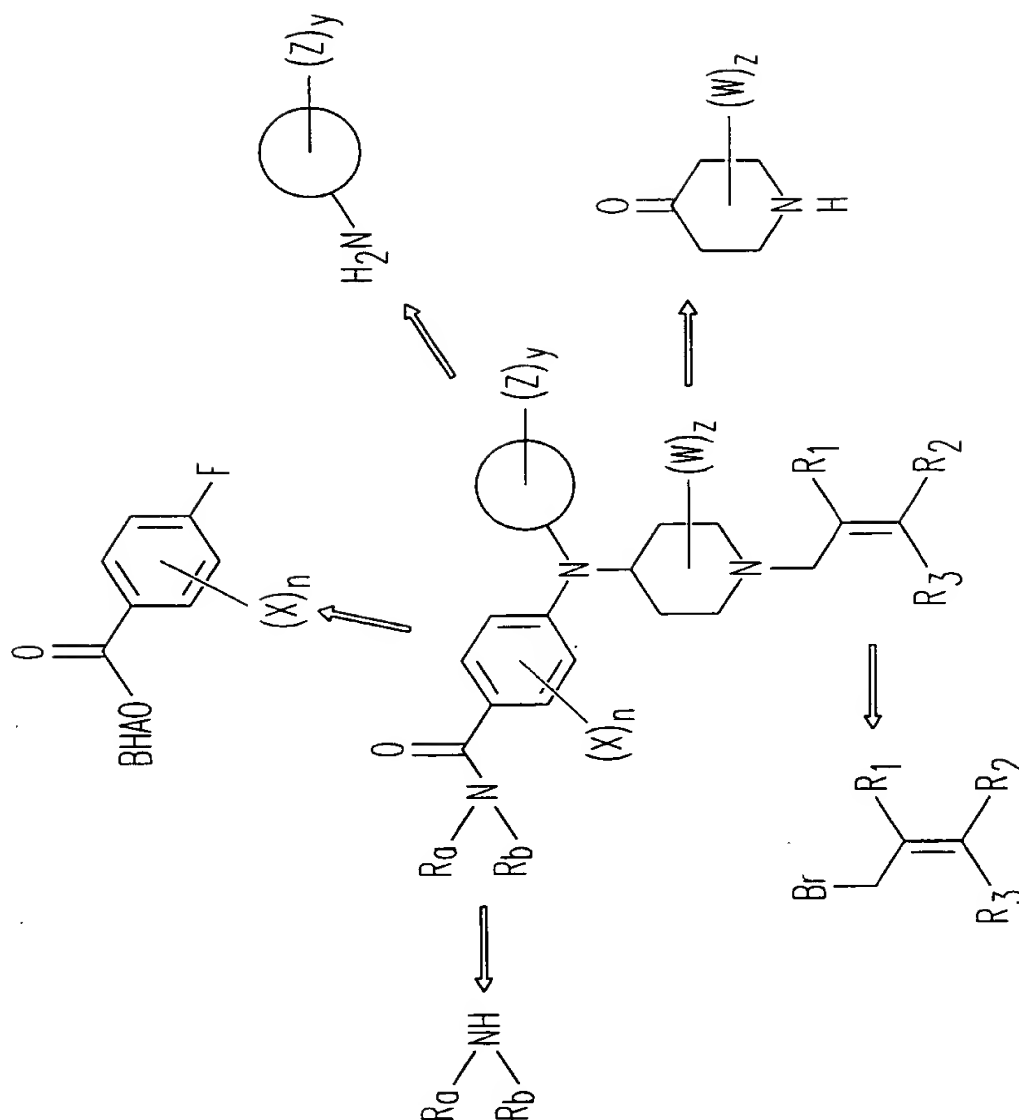
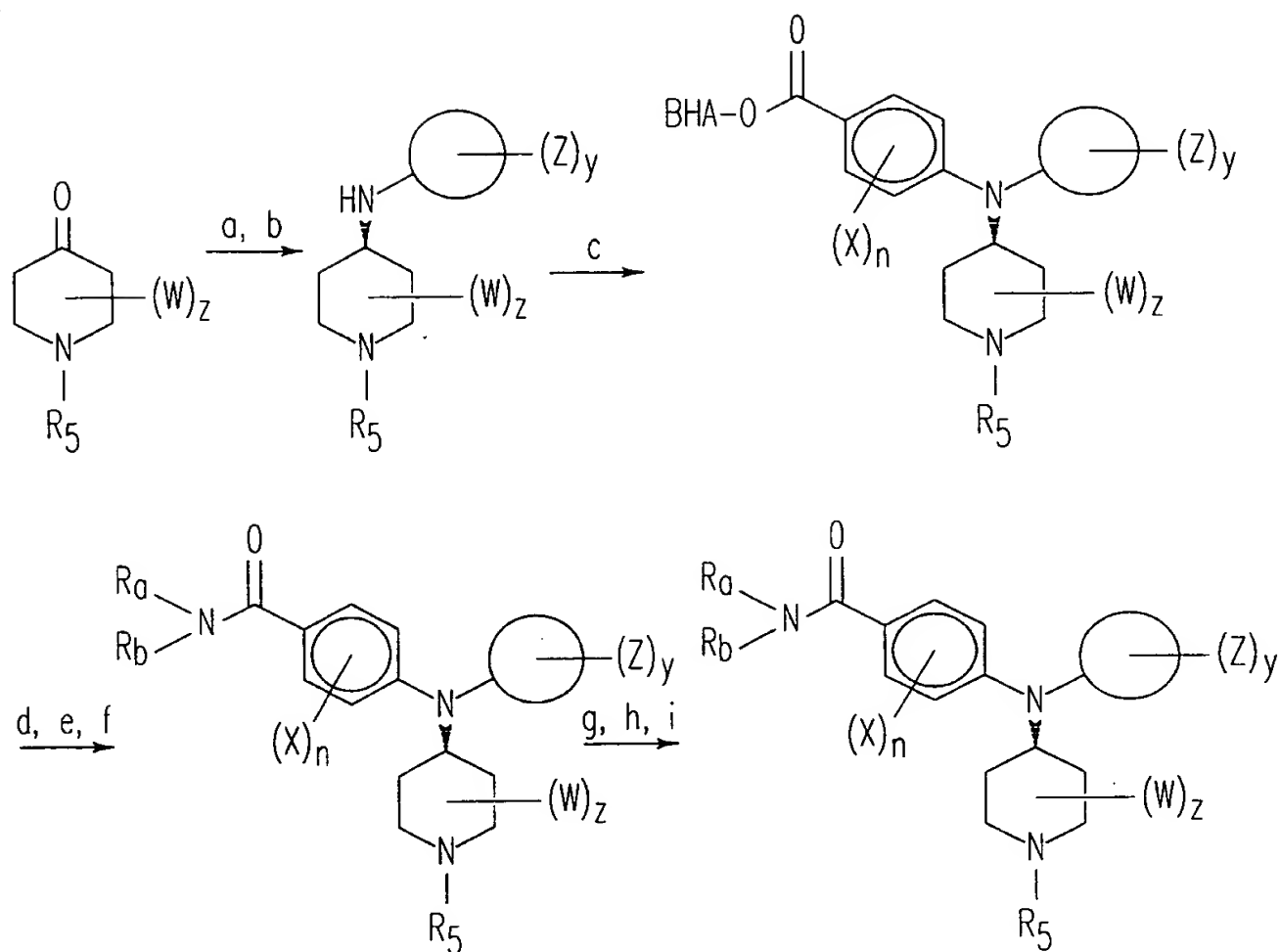


FIG. 3

FIG. 4



Reagents: (A)  $Ti(O-i-Pr)_4$ ,  $:NH-(Z)_y$

(b)  $NaBH_4$ , EtOH;

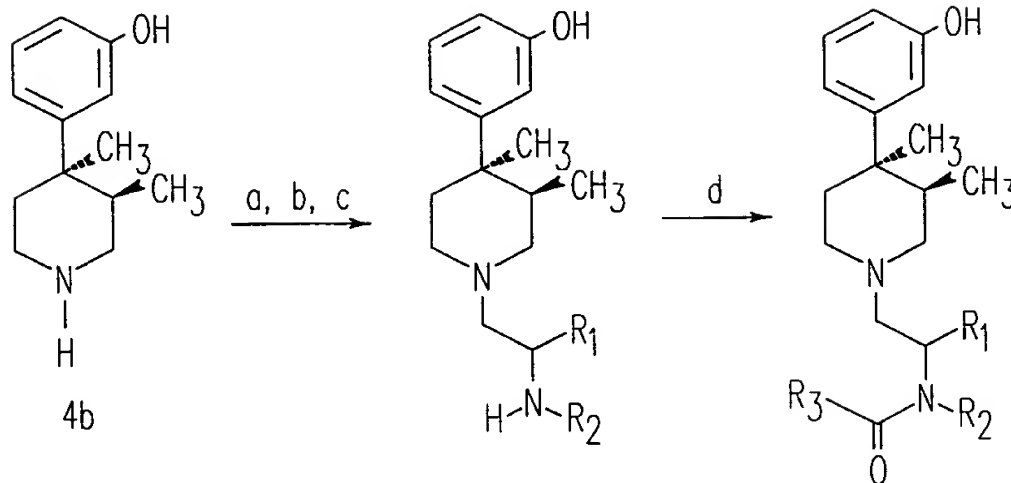
(c)  $n-BuLi$ , THF, HMPA then 1-(2,6-di-tert-butyl-4-methoxy)-4-fluorobenzoate;

(d) N-methylpyrrolidinone,  $NaOCH_3$ , toluene; (e) EtOH,  $H_2O$ ;

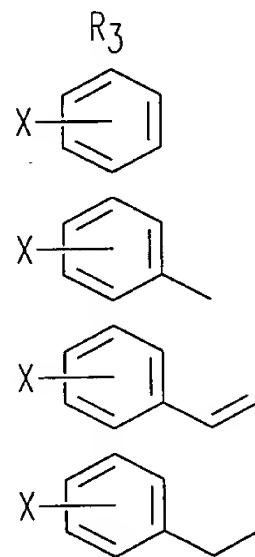
(f)  $R_aR_bNH$ , BOP,  $Et_3N$ ; (g)  $PhOCOCl$ ;

(h)  $KOH$ ,  $i-PrOH$ ,  $H_2O$ ; (i)  $R_5-Br$ , EtOH,  $K_2CO_3$

FIG. 5



	R <sub>1</sub>	R <sub>2</sub>
6a,	H	H
b,	H	CH <sub>3</sub>
c,	CH <sub>3</sub>	H
d,	CH <sub>3</sub>	CH <sub>3</sub>
e,	i-Pr	H
f,	i-Pr	H
g,	i-Bu	H
h,	s-Bu	H
i,	c-Hex	H
j,	Ph	CH <sub>3</sub>
k,	Bn	H



X=OH, OMe, OEt, OBn,  
OnBu, OPh, Me, iPr, Bu,  
Ph, NMe<sub>2</sub>, CONH<sub>2</sub>, F, Cl, Br.

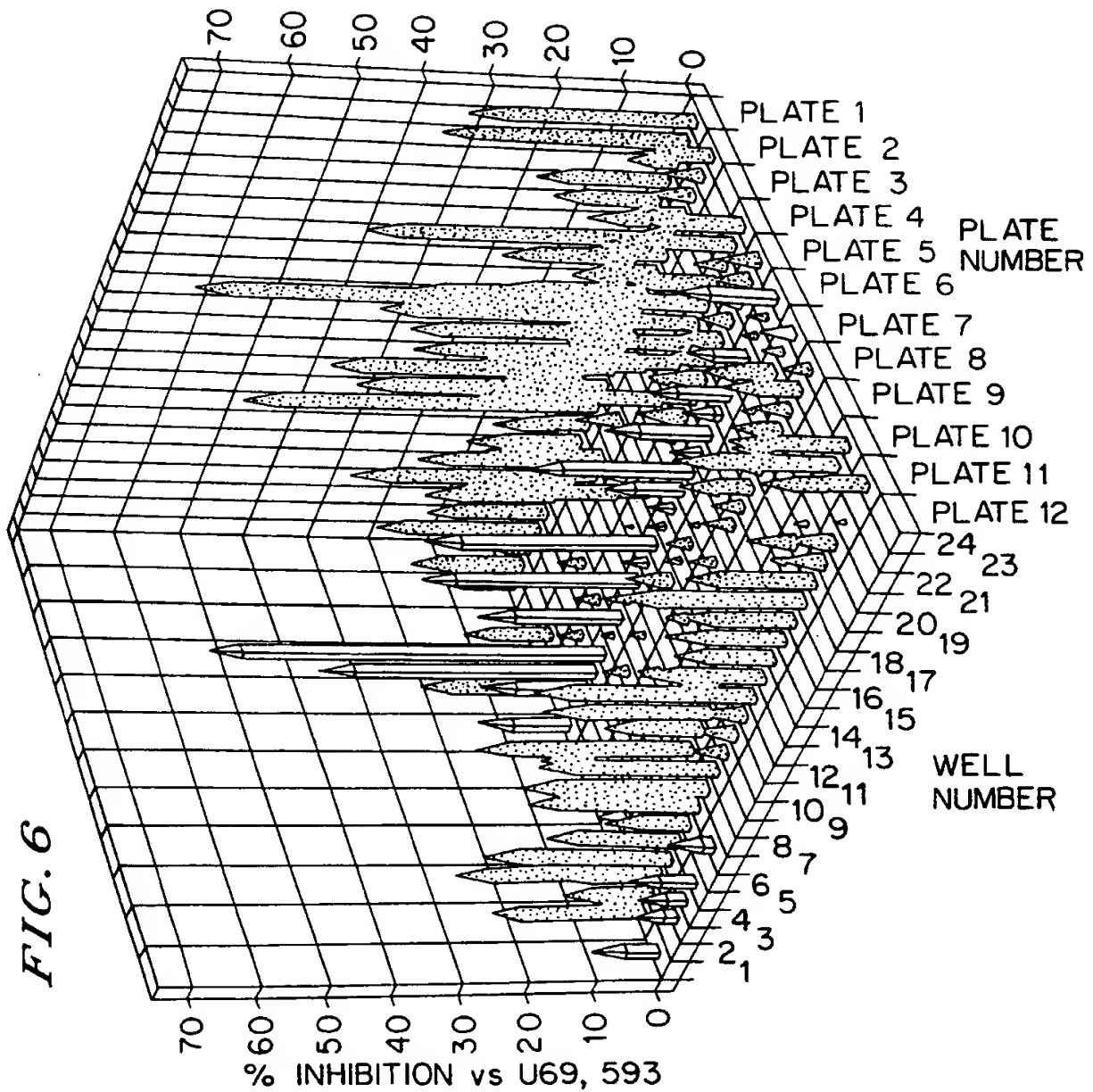
<sup>a</sup>Reagents: (a) Boc-amino acid, BOP, TEA, THF;

(b) TFA, CH<sub>2</sub>Cl<sub>2</sub>;

(c) borane/dimethyl sulfide;

(d) R<sub>3</sub>CO<sub>2</sub>H, BOP, TEA, THF.

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FIG. 7

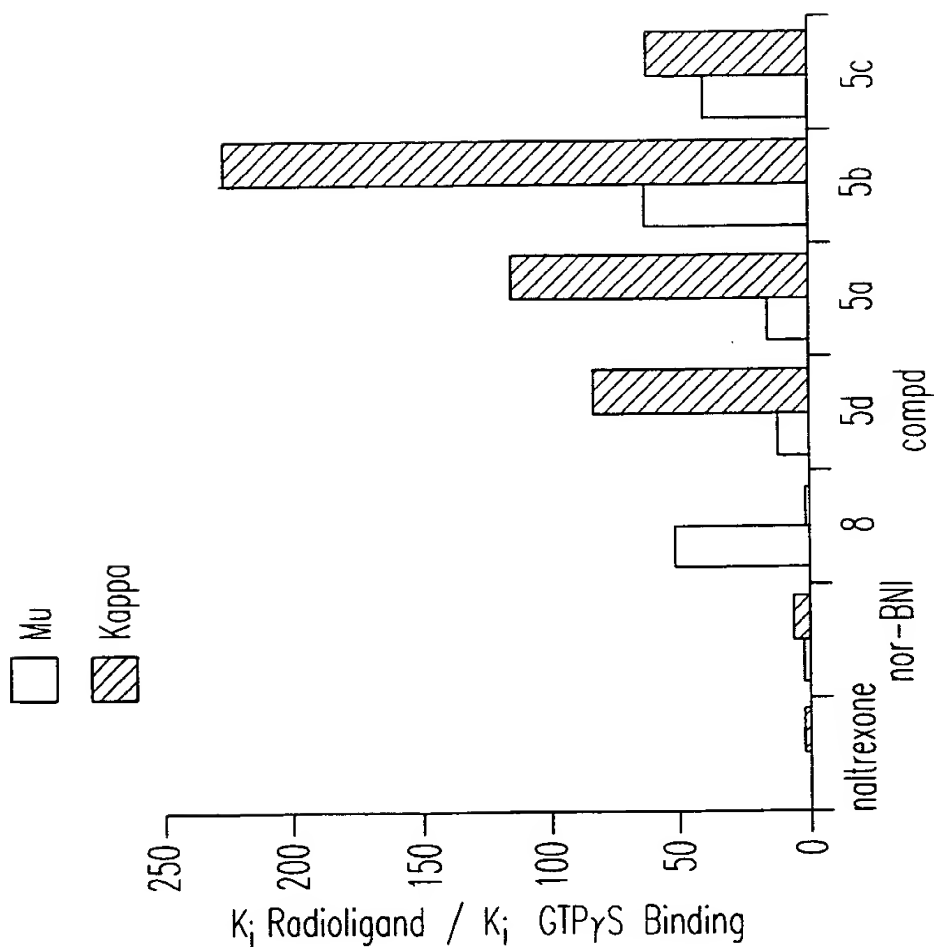
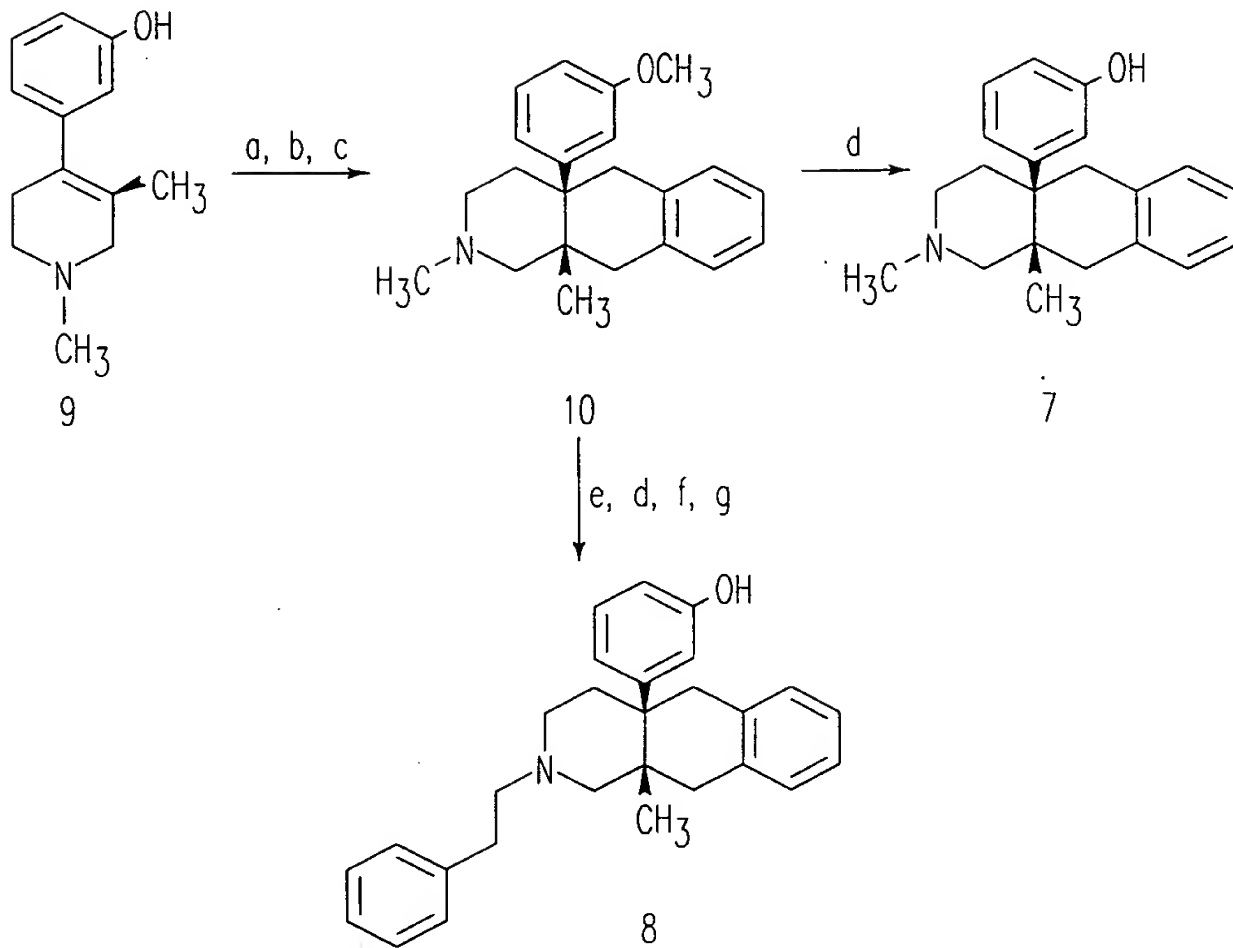


FIG. 7



FIG. 8

(a)  $s\text{-BuLi}$ , THF;  $\alpha,\alpha'$ -dichloroxylene;(e)  $\text{PhOCOCl}$ , toluene;(b)  $\text{NaI}$ ,  $\text{CH}_3\text{CN}$ ;

(f) Phenyl Acetic Acid, BOP, TEA, THF;

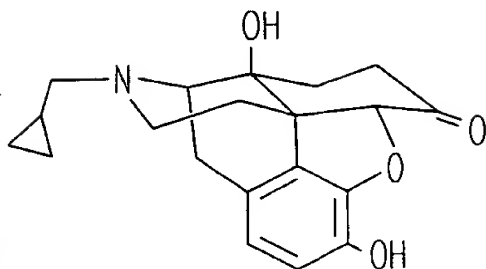
(c)  $\text{NaBH}_4$ , EtOH;

(g) Borane/THF;

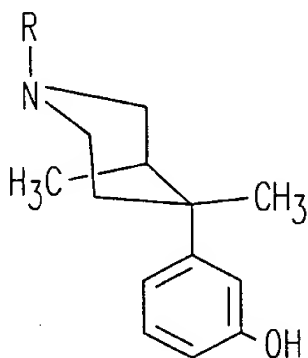
(d)  $\text{HBr}$ ,  $\text{HOAc}$ ;

**FIG. 9A**

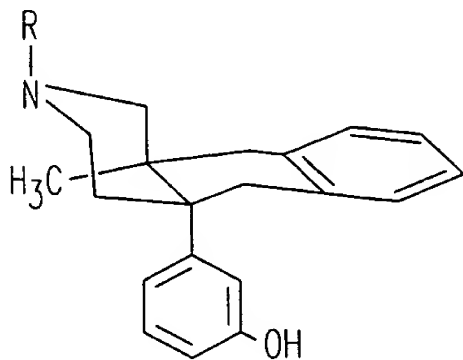
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Naltrexone  
(phenylaxial/piperidine chair)

**FIG. 9B**

3,4-Dimethyl-4-(3-hydroxyphenyl)piperidine  
(phenylequatorial/piperidine chair)

**FIG. 9C**

8a-Methyl-4a-(3-hydroxyphenyl)octahydrobenzo[e]isoquinoline  
(phenylequatorial/piperidine chair)

APPROVED	D.G. FIG.
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FIG. 10

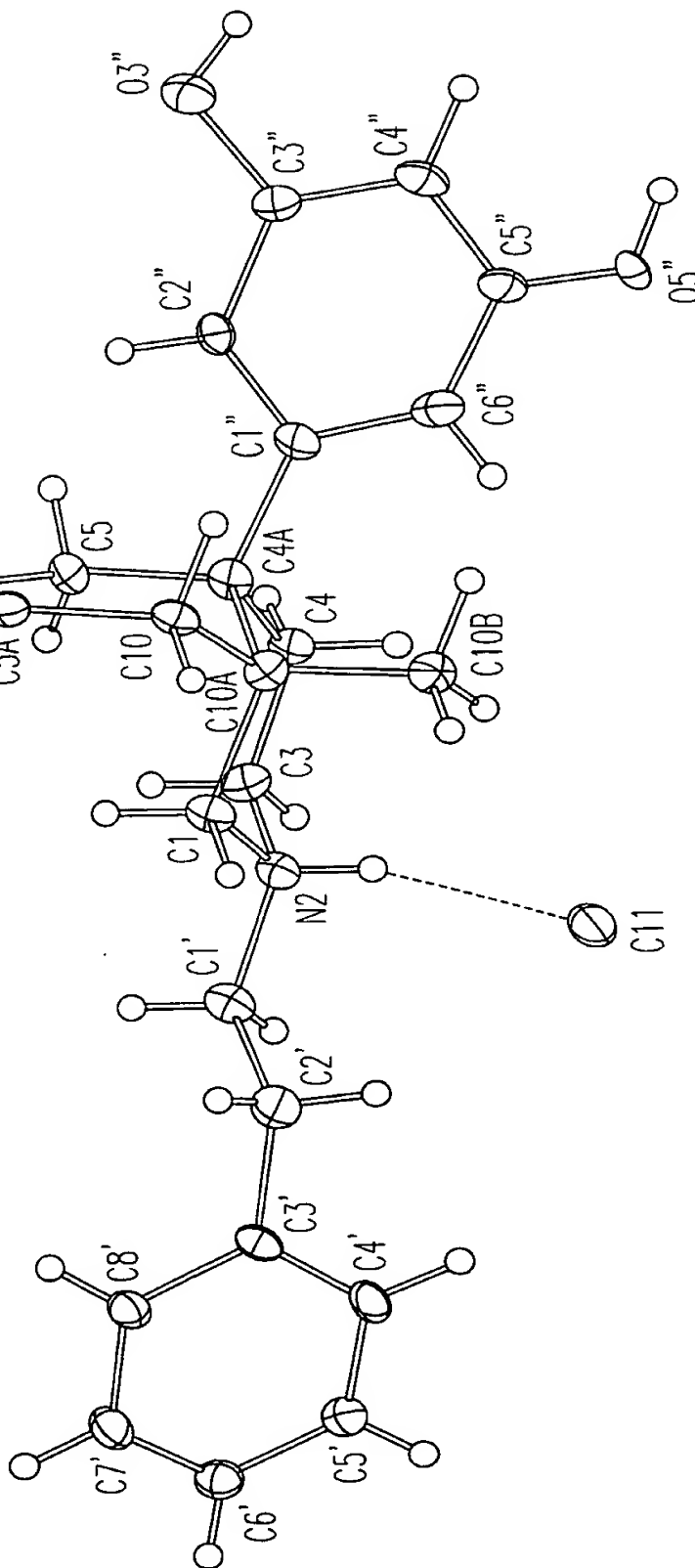
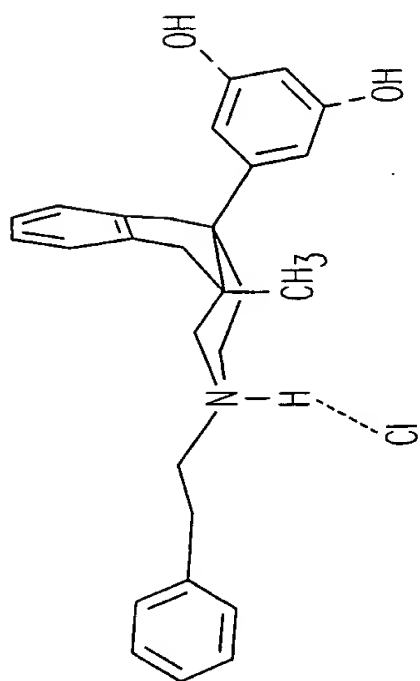
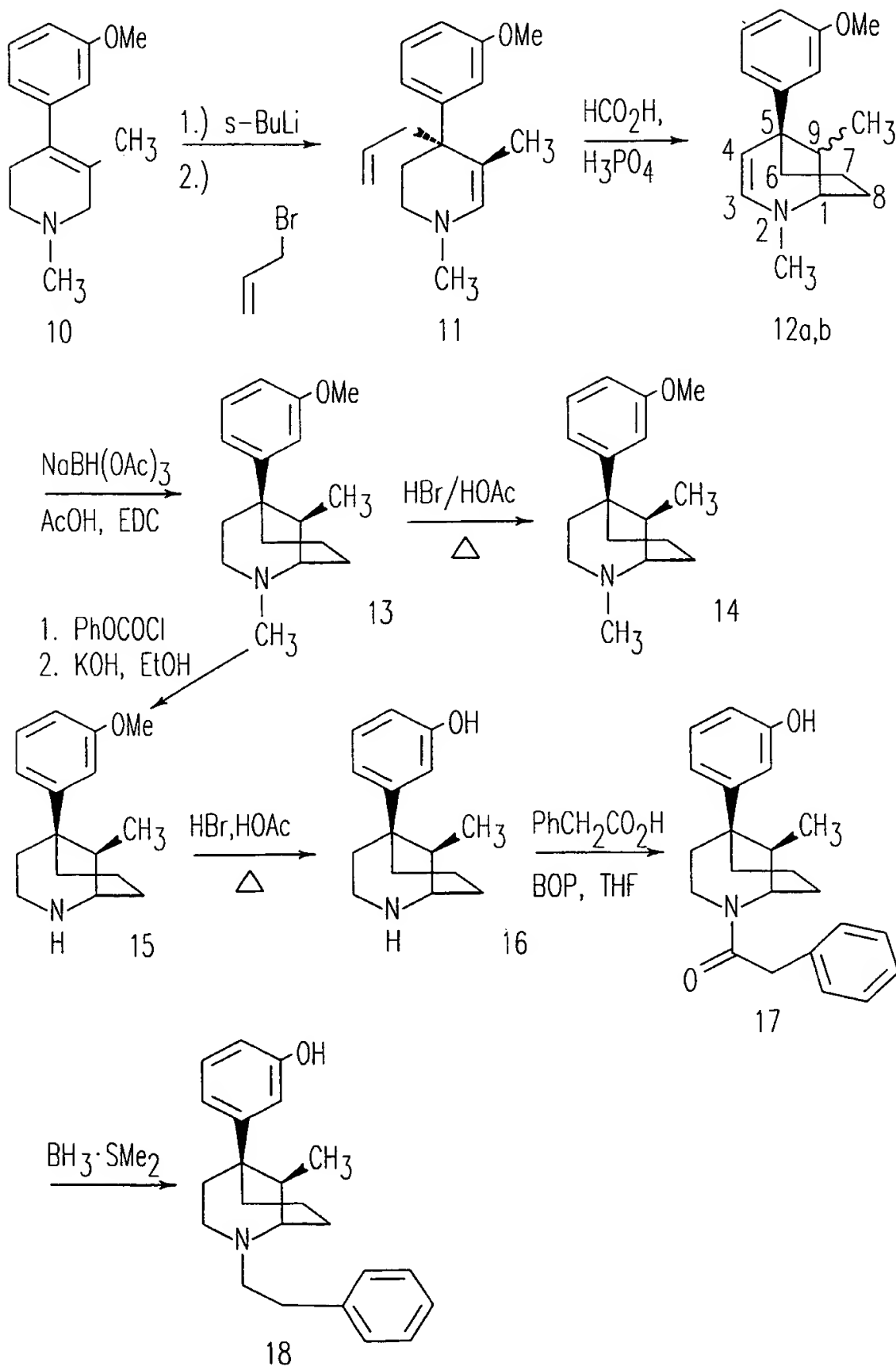


FIG. 10

FIG. 11



APPROVED	J.G. FIG.
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FIG. 12

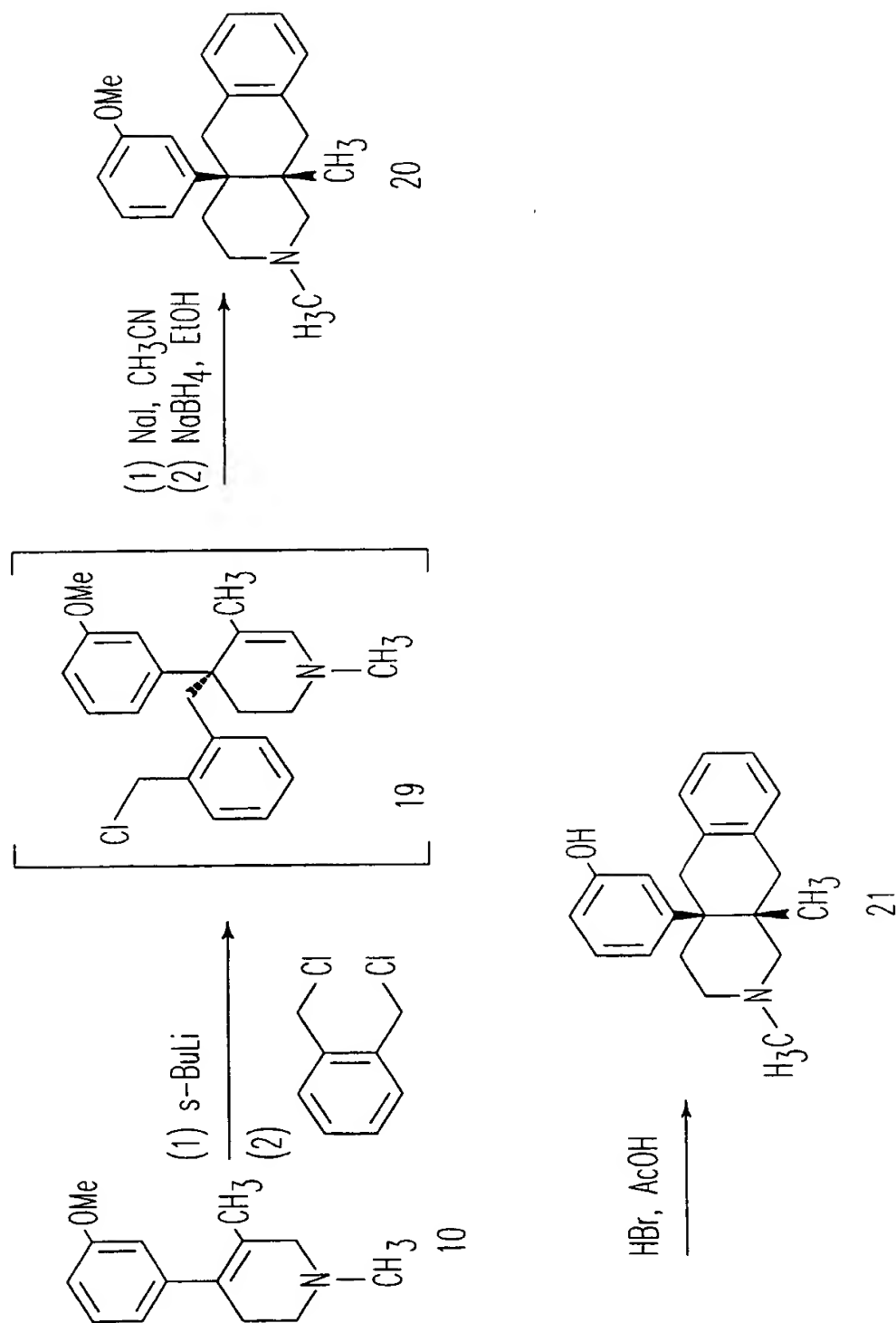
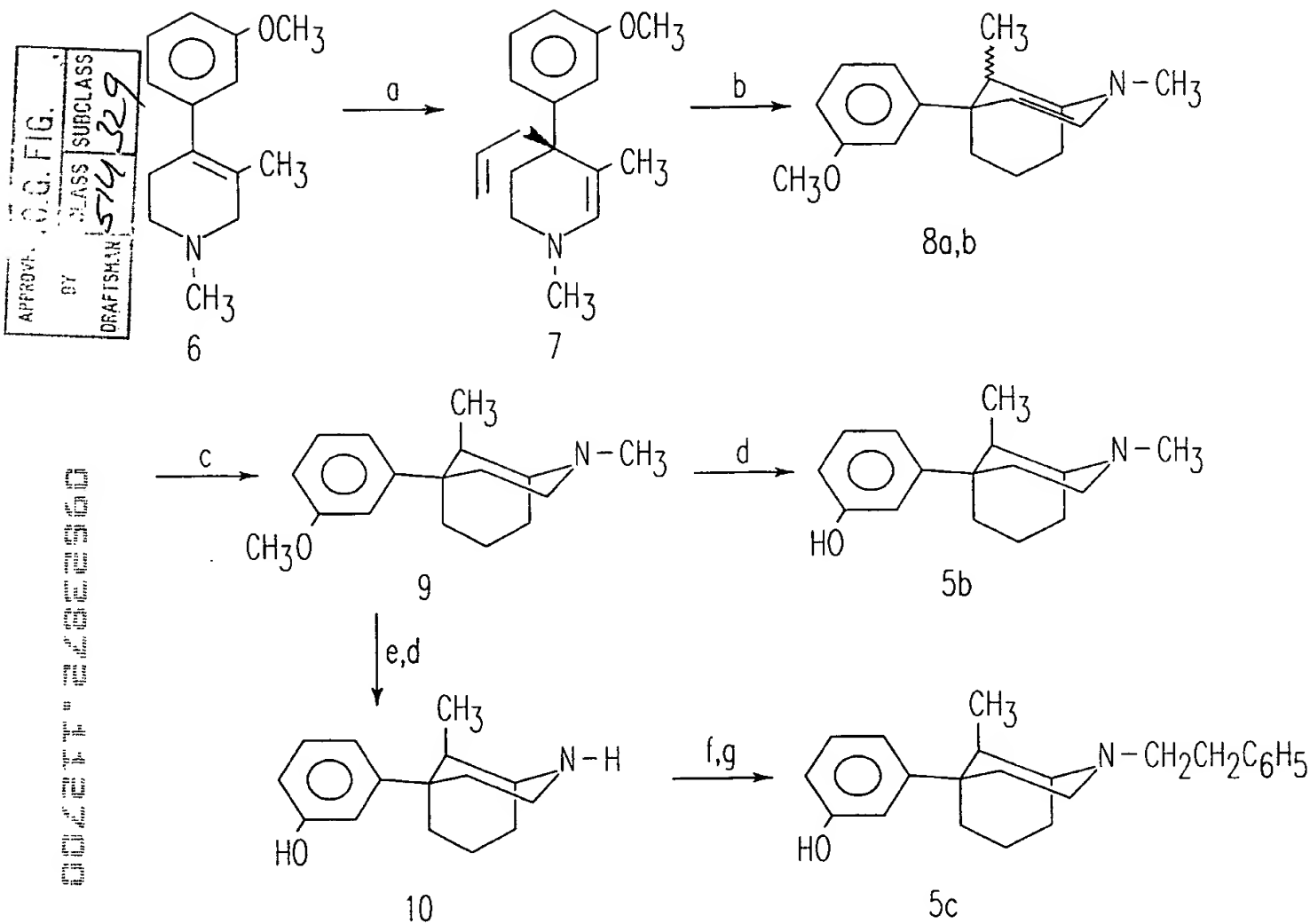


FIG. 13

<sup>a</sup> (a) *s*-BuLi, allyl-Br;(b) H<sub>3</sub>PO<sub>4</sub>, HCO<sub>2</sub>H;(c) NaHB(OAc)<sub>3</sub>;

(d) HOAc, HBr;

(e) PhOCOCI, then KOH, H<sub>2</sub>O;(f) (benzotriazol-1-yloxy)tris(dimethylamino) phosphonium hexafluorophosphate, PhCH<sub>2</sub>CO<sub>2</sub>H;

(g) borane-dimethyl sulfide, THF.

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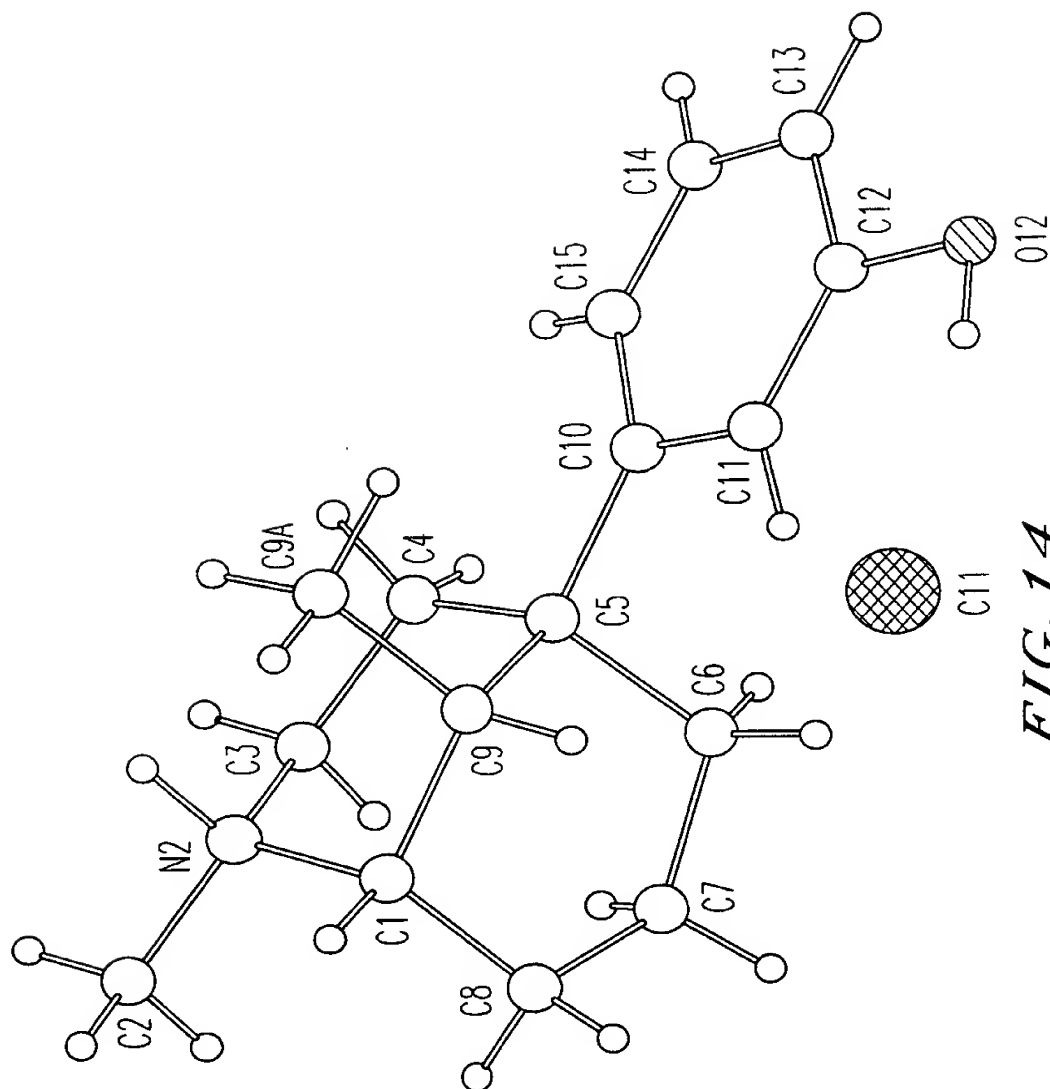
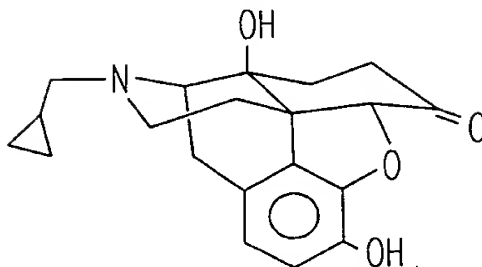


FIG. 14

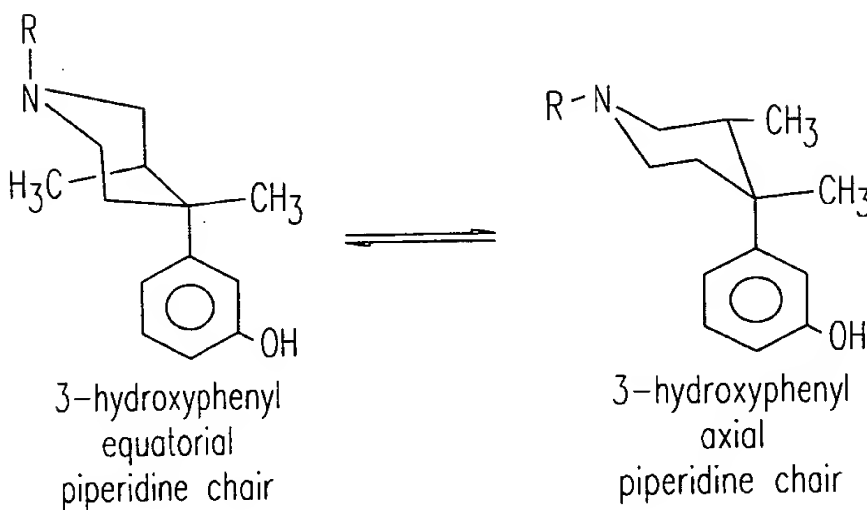
FIG. 15

Naltrexone (1b)

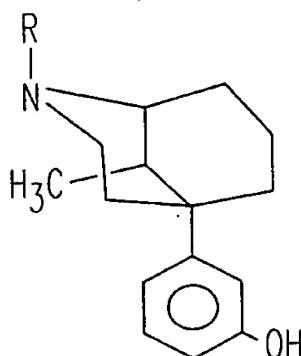


3-hydroxyphenyl axial piperidine chair

3,4-Dimethyl-4-(3-hydroxyphenyl)-piperidine (4)



2-Alkyl-9 $\beta$ -methyl-5-(3-hydroxyphenyl)-  
morphan (5)



3-hydroxyphenyl equatorial piperidine chair

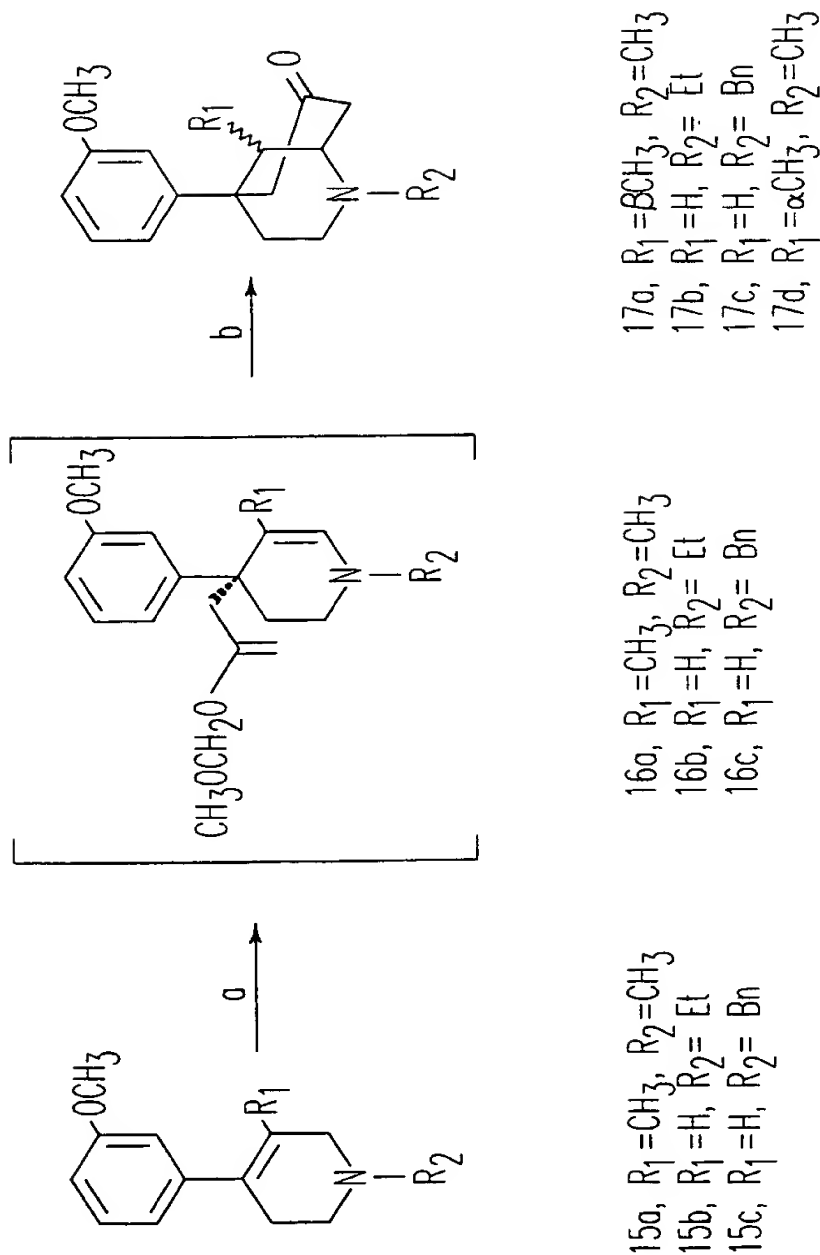
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[illegible]



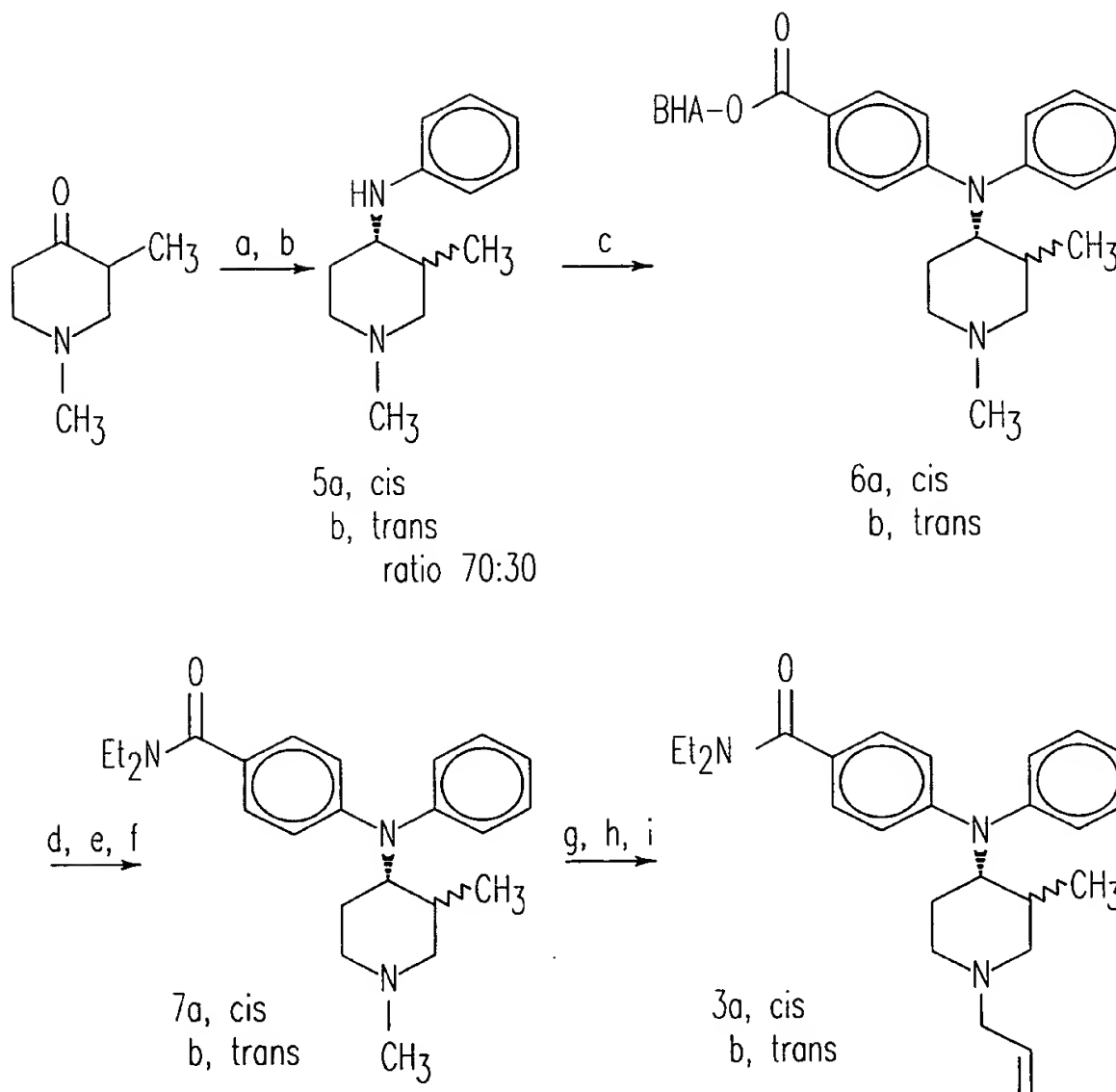
APPROVED	U.R. FIG.
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FIG. 16



18

FIG. 17



Reagents: (a)  $\text{Ti}(\text{O}-i\text{-Pr})_4$ , aniline; (b)  $\text{NaBH}_4$ , EtOH; (c)  $n\text{-BuLi}$ , THF, HMPA then 1-(2,6-di-tert-butyl-4-methoxy)-4-fluorobenzonate; (d) N-methylpyrrolidinone,  $\text{NaOCH}_3$ , toluene; (e) EtOH,  $\text{H}_2\text{O}$ ; (f)  $\text{Et}_2\text{NH}$ , BOP,  $\text{Et}_3\text{N}$ ; (g)  $\text{PhOCOCI}$ ; (h)  $\text{KOH}$ ,  $i\text{-PrOH}$ ,  $\text{H}_2\text{O}$ ; (i) allyl-Br, EtOH,  $\text{K}_2\text{CO}_3$

APPROVED	C.G. FIG.
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FIG. 18

